TB MED 183

WAR DEPARTMENT TECHNICAL BULLETIN

VISCERAL LEISHMANIASIS—KALA-AZAR

War Department, Washington 25, D. C. • • • July 1945

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This bulletin supersedes paragraph 13, SGO Circular Letter No. 33, 1943

1. INTRODUCTION. *a. General.* Leishmaniasis is infection with protozoan organisms of the genus *Leishmania* which is transmitted by *Phlebotomus* sandflies. Many authorities today group all cases into one of two categories, visceral leishmaniasis, which is infection with *Leishmania donovani*, and cutaneous leishmaniasis, which is due to *Leishmania tropica* or *Leishmania braziliensis*. These organisms cannot be separated by any available procedure, but the distinction is considered necessary on epidemiological and pathological grounds. There is no longer any basis for the separate classification of visceral leishmaniasis in infants, which was formerly attributed to "*Leishmania infantum*." Canine leishmaniasis ("*L. caninum*") probably represents merely an epidemiologic variety of *L. donovani* infection. Whereas cutaneous leishmaniasis usually involves only the skin and subcutaneous tissue and, in some cases, the nasopharyngeal mucosa and submucosa, visceral leishmaniasis always causes widespread lesions. The remainder of this bulletin is devoted to visceral leishmaniasis or, as it is commonly known, kala-azar. These terms will be used interchangeably.

b. Incidence. So far as is known, there is no natural immunity to kala-azar. Although the disease is uncommon in individuals of Caucasian origin in India and China, the low incidence is due apparently to infrequent exposure to the disease. Kala-azar is often sporadic in its occurrence, but it may appear in epidemic form. The disease is particularly common in villages, although it also occurs in cities. In India and China there are particular villages and even individual houses which are known to be foci of kala-azar. Those infected belong predominantly to the lower social groups of the population. Statistics show a higher incidence in males, but it is doubtful that they are reliable, since far more males than females attend hospitals in the Orient. Kala-azar is predominantly a disease of young people, but it is also common in the third decade of life and may occur at any age. In the Mediterranean area the incidence in infants is said to be relatively higher than it is in other areas. Many animals, including especially the hamster, are susceptible to artificial infection, but the

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only animal found to be infected in nature is the dog.

2. GEOGRAPHIC DISTRIBUTION. Visceral leishmaniasis is found in Asia, Africa, Europe, and South America (fig. 1). The incidence varies greatly even in contiguous areas.

a. China. The disease is common in many of the provinces north of the Yangtse River. It is especially prevalent in parts of Kiangsu, Shantung, Honan, Hopei, Anhwei, and Shensi. It is also found in Hupei, Shansi, Szechwan, Kansu, and southern Manchuria (Manchukuo). South of the Yangtse River, a few cases are found in Kiangsu, Chekiang, Kiangsi, and Kwangsi. There is one doubtful report of cases in Canton.

b. India. Kala-azar is found in parts of the eastern portion of the country, including Madras Presidency, Orissa, the United Provinces, and is especially common in Bihar, Bengal, and Assam.

c. Other parts of eastern Asia. The disease has not been reported in Korea, the Japanese Empire, Formosa, the Philippines, Malaya, the Netherlands East Indies, or Burma.

d. Russia. Kala-azar exists in parts of Russian Turkestan and southern European Russia.

e. Mediterranean Area. Kala-azar is found with varying incidence in all the countries bordering on the Mediterranean, especially in parts of Greece, Crete, Yugoslavia, southern Italy, Sicily, Malta, and southern France. It is less frequent, but present, in Palestine, Syria, Turkey, Spain, and North Africa. Cases have been reported in Portugal.

f. Africa. In addition to North Africa (*e* above), kala-azar exists in the Sudan, Ethiopia, Eritrea, Kenya, French Equatorial Africa (Lake Chad region and Gabon), and Nigeria.

g. South America. Visceral leishmaniasis occurs in northern Argentina, Paraguay, and eastern and northern Brazil.

3. ETIOLOGIC AGENT. *a. General.* *Leishmania donovani*, the causal organism of visceral leishmaniasis, is a protozoan parasite which belongs to a group known as hemoflagellates that inhabit the blood or other tissues of vertebrates. Two forms of *Leishmania donovani* are present in its life cycle, the leishmania form—a stage lacking a flagellum—which occurs in man or other mammalian hosts, and a leptomonad or flagellate form which develops in the sandfly intermediate host and in artificial culture media.

b. Leishmania forms. These forms, commonly referred to as Leishman-Donovan bodies, are small ovoid or round unicellular organisms measuring 2 to 4 microns in diameter, which occur in reticulo-endothelial cells and macrophages. The parasites are characterized by a relatively large rounded nucleus usually located on one side of the body and a kinetoplast which appears either as a minute dot or tiny oblique rod (fig. 2). In well-stained specimens, the kinetoplast may be seen to consist of a rodlike parabasal body and a dotlike blepharoplast. Elongated slender "torpedo forms" with blunt or pointed ends may also be observed in man. With Giemsa or Wright's stain, the cytoplasm appears pale blue and the nucleus and kinetoplast red or reddish purple. The leishmania forms grow and multiply at the expense of the host cells which they parasitize. Infected cells become enlarged and finally disintegrate. The liberated parasites are taken up by other endothelial cells or are phagocytosed by polymorphonuclear leukocytes. The organisms are abundant in certain tissues and are present in small numbers in monocytes in the circulating blood.

c. The leptomonad form. These forms result from a transformation which the leishmania forms undergo in the digestive tract of sandfly vectors after they have fed on an infected vertebrate host or in cultures when inoculated on suitable media. The leptomonad forms are spindle-shaped bodies 14 to 20 microns long by 1.5 to 3.5 microns broad, with a more or less centrally placed nucleus (fig. 3). They resemble trypanosomes in shape, but lack an undulating membrane. The flagellum is as long as or longer than the body, and originates from a kinetoplast which lies transversely at the anterior end of the organism. The flagellate forms multiply by longitudinal fission and may be maintained indefinitely in culture. In young cultures, stumpy pear-shaped or oval forms may be common. The leptomonad form moves actively with the flagellum foremost. In cultures,

the leptomonads frequently tend to agglomerate in rosette groups with their entangled flagella directed inwards. Leptomonads may be observed in the midgut of Phlebotomus sandflies by the third day after the leishmania forms have been taken up from an infected mammalian host. As they multiply, the leptomonads move forward to occupy an anterior station in the pharynx and buccal cavity of the sandfly. The leptomonads are presumed to gain access to man when the flies subsequently feed. Inside the body they undergo transformation and multiply as intracellular leishmania forms.

4. TRANSMISSION. *a. The vector.* Sandflies of the genus *Phlebotomus* are chiefly responsible for the transmission of visceral leishmaniasis. These minute blood-sucking vectors are hairy, moth-like insects, capable of penetrating standard mosquito netting and screening. They should not be confused with species of *Culicoides* (gnats or midges) which also are commonly referred to as sandflies. *Phlebotomus* species are weak fliers, having a flight range, at most, measuring a few hundred yards. Consequently, these sandflies are most numerous in the immediate vicinity of their breeding places. The larvae develop in dark, slightly moist places, such as crevices in walls, floors, masonry ruins, under rocks or rubble, in sandy soil, in caves, and along river banks. Larval development requires from several weeks to several months, depending upon the temperature. Daytime shelters for adult sandflies include breeding sites, and also tree hollows and buttresses, animal burrows, and dark sections of human or animal habitations. The average length of life of adult sandflies is estimated to be from 2 to 3 weeks. As with mosquitoes, only the females feed on man or animals. Sandflies are nocturnal feeders, most active on warm, still nights. They attack silently, seeking out the ankles, wrists, knees, and elbows. Often the bites cause a severe local reaction. The recognition of sandflies is aided by their irregular flight with short hops and long pauses and the elevated V-position assumed by the wings when the insects are at rest. Sandflies seldom rise as high as the second floor of a building.

b. Important species. *Phlebotomus argentipes* is considered the most important vector in India, *P. chinensis* in China, and *P. perniciosus* in the Mediterranean region. Some of the species of sandflies commonly associated with the transmission of kala-azar are listed below:

India: *P. argentipes.*
China: *P. chinensis; P. sergenti* var. *mongolensis.*
Mediterranean: *P. perniciosus; P. major.*
Spain: *P. papatasii.*
Palestine: *P. perfilewi.*
N. Africa: *P. sergenti.*
Sudan, Ethiopia: *P. langeroni* var. *orientalis.*
Brazil, Paraguay: *P. intermedius* (*lutzi*); *P. longipalpis.*

c. The reservoir of infection. In many endemic areas it is probable that man constitutes the important reservoir of infection. In certain areas, such as China, the Mediterranean, and South America, where natural canine infections occur, dogs also may play a part in the epidemiology of kala-azar. Hamsters, and certain other lower animals although susceptible to infection experimentally, are not known to harbor naturally acquired infection.

d. Other possible modes of transmission. Since leishmania forms have been demonstrated in nasal and pharyngeal secretions, urine, and stools of kala-azar patients, the possibility that the parasite may be transmitted through contamination of food or drink, by droplet infection, or by contact, cannot be completely disregarded. However, these modes of infection probably play a minor role, if any, in the spread of the disease.

5. CLINICAL PICTURE. *a. General.* Little is known concerning the dissemination of the parasites immediately following infection. Presumably, the parasites are rapidly spread to many parts of the body. At post-mortem examinations, they are found in endothelial cells in many organs, including the skin, and, especially, the spleen, liver, bone marrow, and lymphoid tissue. The disease is regarded as a reticulo-endotheliosis.

b. Incubation and onset. The incubation period is variable, extending from 2 weeks to 18 months. In the majority of cases, it is believed to be within 2 to 6 months. The onset is also variable. Sometimes it is very slow and insid-

ious, and sometimes it is well defined with a gradual development of high fever over a period of 5 to 7 days, as often happens in typhoid fever. In unusual instances the onset is sudden, with high fever, chills, nausea, and vomiting.

c. Symptoms. There is nothing characteristic about the symptoms of kala-azar. In many instances symptoms are of the vaguest sort for many weeks, suggesting the picture often seen in incipient pulmonary tuberculosis. The degree of prostration is frequently remarkably slight. In one large series of early cases, the symptoms in order of frequency were fever, chills, dizziness, headache, anorexia, cough, sweating, constipation, weakness, loss of weight, diarrhea, malaise, epistaxis, abdominal discomfort, nausea and vomiting, and bleeding gums. In rare instances, attacks of pain occur in the splenic region. In children, irritability, mental clouding, and, rarely, convulsions may appear.

d. Fever. The temperature curve assumes a variable form. It usually shows an irregular remittent or intermittent fever. In some cases, however, fever is well-sustained, and the chart shows an uneven plateau. Occasionally, there are wide swings of temperature, such as occur in septicemia. Double and even triple rises in temperature during a single 24-hour period have been described as characteristic, and should lead one to think of the disease, but they are absent in two-thirds of the cases, and even when present they cannot be considered to be pathognomonic, since they occur in other infections.

e. Physical signs. Patients often do not appear as ill as the temperature would indicate, and in early cases the general examination may reveal little. Enlargement of the spleen is characteristic of established infections with kala-azar. It is an error to suppose that the spleen is necessarily huge, however, since the diagnosis may be made when the spleen is not palpable and is often made when it projects only slightly beyond the costal margin. It should be noted that when the spleen becomes very large it sometimes lies in a horizontal position and sometimes lies vertically. The liver is also enlarged, but the enlargement appears to take place somewhat later than that of the spleen. Tenderness of spleen or liver is unusual. Jaundice and ascites are rare, and when present are perhaps not directly due to kala-azar. An important finding in some cases is enlargement of lymph nodes (the enlargement has no characteristic distribution). Other physical signs are of less importance and are associated chiefly with progressive advance of the disease beyond the early stage. After kala-azar has been active for weeks or months, wasting appears. When blood changes are advanced, pallor and other signs of anemia may be seen. Purpura is an occasional feature. Petechiae are rare and rose spots do not occur. In time, the skin tends to acquire a dusky hue, especially in patients with a dark complexion, but the change is often difficult to make out. The skin may become coarse and dry, and the hair may become scanty. In unusual instances, found for the most part among patients who have been treated inadequately, specific skin lesions may develop. These constitute the so-called post-kala-azar dermal leishmanoid. They occur occasionally on the trunk, but usually on the cheeks and nose (where they may take on a "butterfly" configuration) or lips. Such lesions are originally macular, but become raised and in time nodular. They are associated with depigmentation and do not break down. They contain Leishman-Donovan bodies. Among the incidental findings may be pulsations in the neck vessels, tachycardia, cardiac murmurs, and low blood pressure. The lungs show nothing characteristic.

f. Blood, urine, and stools. The urine and stool show nothing remarkable. The changes in the blood, which are of the greatest importance, are described in paragraph 6*b*.

g. Complications. Patients with kala-azar appear to be peculiarly susceptible to other infections. Stomatitis is common in neglected children. Once established, oral infection may result in noma or cancrum oris, a well-nigh intractable condition. Bronchitis and pneumonia are the commonest secondary infections. In a few instances, nephritis may appear, probably not as a result of kala-azar itself. In advanced cases, edema may be seen, usually because of plasma albumin deficiency.

h. Course. The clinical manifestations usually develop slowly but progressively. In many

cases, the patients have minor symptoms for weeks without reporting sick. Without treatment, the disease usually runs a course, with remissions and relapses, for a period of 2 years or more. During remissions patients may feel, and appear to be, well. In some epidemics, especially in the Sudan areas, the course is relatively fulminating.

6. DIAGNOSIS. *a. Clinical diagnosis.* The diagnosis should always be confirmed by demonstration of the parasite (*c* below). A "therapeutic test" is not considered satisfactory evidence of the disease. The outstanding considerations, apart from demonstration of the parasite, are exposure to the disease, the type of onset and temperature curve (par. 5*d*), palpable spleen and usually palpable liver, and the blood changes (*b* below). Malaria is probably the most frequent source of diagnostic confusion. The two diseases should be separated by parasitologic studies. Other diseases which may need differentiation from kala-azar are schistosomiasis (eggs in stools or urine), relapsing fever (spirochetes in blood), leptospirosis or Weil's disease (agglutination tests, spirochetes obtained by animal inoculation), typhoid fever (blood cultures, agglutination tests), undulant fever (blood cultures, agglutination tests), septicemic conditions such as bacterial endocarditis (blood cultures), pulmonary or abdominal tuberculosis, histoplasmosis, Hodgkin's disease, Banti's syndrome, and blood diseases, especially aleukemic leukemia.

b. Blood studies. (1) The changes in the blood in kala-azar are extremely helpful in diagnosis. The earliest change is a fall in the total leukocyte count, which is due largely to a decrease in granulocytes. While this decrease is not invariably present, it is found in about 80 percent of the cases. Patients with kala-azar may respond to another infection with leukocytosis, but in such cases the leukocytosis is rarely marked. In occasional instances, agranulocytosis develops. There is no eosinophilia. The erythrocyte count falls with varying rapidity. Early cases may be diagnosed before anemia is present, but in established infections anemia is the rule. It may be very severe. Red blood cells tend to be large and hyperchromic. Nucleated forms are unusual. Platelets are also decreased more or less in proportion to the progress of the disease.

(2) The erythrocyte sedimentation rate tends to be increased and may reach high values. The clotting time also tends to increase, but usually is not greatly prolonged. In advanced cases, the bleeding time may be increased.

(3) The plasma proteins undergo a marked change which results in reversal of the albumin-globulin ratio. The globulin fraction begins to increase early in the disease and later may reach extreme values, such as 6 or 8 grams per 100 cc. In advanced cases, the albumin fraction may be much reduced. The relationship of these changes to the qualitative tests which are described below is uncertain. None of these tests is believed to be specific for kala-azar (they are often positive in schistosomiasis and occasionally in other diseases, including malaria). All of these tests may be negative in very early cases which are proved by demonstration of the parasite. Nevertheless, in conjunction with other data, the tests are extremely useful.

(*a*) *Aldehyde test.* To 1 cc of fresh clear serum, add 1 or 2 drops of commercial formalin. A strongly positive reaction is shown by the development within a few minutes of complete opacity and solidification. If complete opacity develops within 24 hours, the result is still positive. Varying degrees of cloudiness indicate doubtful results. When the serum remains clear, the result is negative, even though it solidifies.

(*b*) *Antimony test.* Dilute a small amount of fresh clear serum ten times with distilled water. Place 2 cc of diluted serum in a test tube 4 or 5 mm in diameter and add from a pipette 2 cc of 4 percent solution of neostibosan in distilled water. Rotate the tube between the palms and then read the result. A heavy flocculent precipitate indicates a strongly positive result, mere cloudiness a doubtful result, and absence of precipitate a negative result. The administration of quinine within 24 hours of the test may cause a false positive result.

(*c*) *Distilled water test.* Obtain, without squeezing, from a skin puncture 20 c mm of blood in a hemoglobin pipette. Empty the blood immediately into a small clean test tube (7 to 8 mm in diameter) containing 0.6 cc dis-

rigidly. If a stylet is in place, it is withdrawn and a sterile air-tight 5 cc syringe attached. Suction is produced until a small amount of blood enters the syringe. The plunger is then gently released and the needle is quickly withdrawn. Pressure should be applied gently with the hand over a sterile pad for a few minutes, after which the abdominal binder is closed. The aspirated material should be used for preparing smears and cultures, as described in (4) and (5) below.

(*e*) The patient should not have solid food for 2 or 3 hours, and he should remain in bed until the next day. He should be observed closely and the pulse and blood pressure should be taken frequently for 24 hours. Appropriate steps should be taken at once, if any evidence of bleeding is observed.

(4) *Smears.* Tissue puncture material should be spread as thin as possible, allowed to dry, and, after staining with Giemsa or Wright's stain, should be examined under an oil immersion lens. The examination of stained preparations of such material gives a high percentage of positive results, but long search may be required to find the parasites. In the preparation of smears, large parasitized mononuclear cells are frequently broken and parasites liberated. As a result, free Leishman-Donovan bodies may be found. These must not be mistaken for platelets and hence disregarded; conversely, platelets should not be identified as Leishman-Donovan bodies. When doubtful objects are seen, further search should be made for parasites which show typical morphology and leave no doubt as to the identification.

(5) *Cultures.* When parasites cannot be found by direct microscopic examination of tissue smears, they may be demonstrable in cultures of the tissue material. Since from 1 to 4 weeks may elapse before the flagellates multiply sufficiently to be detected, cultures cannot be relied upon to establish a diagnosis promptly. However, they should be employed routinely whenever possible. They should be used also to confirm the diagnosis of leishmania forms observed in tissue smears. Since the parasites occur in small numbers in monocytes in the peripheral blood, culture of the leukocyte layer of 10 cc of centrifuged citrated blood sometimes may give a positive result. In the case of puncture material, after a smear is made, a few drops of sterile saline solution should be taken up into the syringe. The resulting mixture is then expelled onto the base of a slant of NNN medium. NNN (Novy-MacNeal-Nicolle) medium containing defibrinated rabbit blood is the most satisfactory medium for cultures (TM 8–227). The technique of cultivation of leishmania demands careful attention to aseptic precautions in securing and inoculating the material, as the organisms will not survive in cultures containing bacteria. Cultures for *L. donovani* should be kept as near 22° C. (71.6° F.) as possible. They should never be put in an incubator at 37° C., since the organisms do not multiply at this temperature. The cultures should be examined for parasites every few days and not discarded until at least a month has passed. Rubber caps or stoppers should be used to prevent the cultures from drying, or small amounts of sterile saline may be added from time to time. A platinum loop may be used for obtaining material for examination of the cultures, using precautions to prevent bacterial contamination. The material should be mixed with a small amount of saline on a slide and the actively motile flagellates searched for in the fresh wet preparation, using the high power of the microscope. If negative, a small amount of water of condensation in the culture may be secured with a capillary pipette and examined in the same way. Morphological detail may be observed in smears of culture material stained by Giemsa's or Wright's method.

7. TREATMENT. *a. General.* Patients with fever, severe anemia, or leukopenia should be kept in bed. A well balanced and liberal diet should be given, unless some complication indicates a special regimen. Fluids should be given freely. Special attention should be paid to the care of the mouth in order to secure and maintain cleanliness. Mouth washes should be bland and nonirritating, especially if any lesions are present. If severe anemia, leukopenia, or bleeding tendency exists, transfusions of blood should be given. In cases with secondary infection or cancrum oris, the use of penicillin is advised. In general, the chemotherapy of kala-azar takes precedence over the specific treatment

of other infections which may be concomitant. Splenectomy should never be performed for the treatment of this disease.

b. Chemotherapy. (1) *General.* The early institution of chemotherapy for kala-azar is highly desirable. There are few contra-indications for such treatment, except serious disease of the lungs, heart, liver (aside from disease due to leishmaniasis), and kidneys. The presence of the usual complications of kala-azar is only a further reason for pressing ahead with chemotherapy. At present, neostibosan is considered the drug of choice for general use. Antimony and potassium tartrate has been used in the past for the treatment of kala-azar, but it is more toxic and less effective than neostibosan, and is not recommended. Fuadin should not be used for the treatment of kala-azar. Many infections acquired in the Sudan and a few acquired elsewhere are resistant to the usual treatment. Stilbamidine, a nonstandard drug, has been recommended for use in such cases. It may be obtained as nonstandard Item 1N77830 Stilbamidine, 0.15 gm, 10 ampules in box; unit—box, only by requisition stating full justification for its need. Requisitions for this item must be forwarded by depots or service commands to The Surgeon General's Office for approval. In the United States, patients who may require treatment with stilbamidine should be transferred to one of the hospitals designated for specialized treatment of tropical diseases. In certain oversea areas, it may be possible to procure this drug—which is exclusively of British manufacture—from British sources by local procurement. Permission for the use of other drugs than neostibosan or antimony and potassium tartrate should be obtained from The Surgeon General or in oversea areas from the theater surgeon. Patients who are under treatment should be kept in bed and should be observed closely.

(2) *Neostibosan.* This drug is a standard Medical Department supply item, catalogue No. 1300700, supply unit 10 ampules, each ampule containing neostibosan 0.3 gm. Medical officers in areas where kala-azar is likely to be encountered should check with supply officers to be sure that stocks of this drug are available; if the drug is not in stock, a requisition should be submitted immediately. Neostibosan is described as consisting of para-amino phenylstibonic acid, para-acetyl-amino phenylstibonic acid, antimonic acid, and diethylamine and as containing 41 to 44 percent antimony. The drug is relatively unstable in solution, and should be given only when *freshly* prepared with sterile distilled water. The solution should not be boiled or heated, and it should be used as soon as possible. Neostibosan is administered intravenously in 5 percent solution. For adults, the first dose is 0.2 gm, and subsequent doses are 0.3 gm. The total dose is 3.8 to 5.0 gm (13 to 16 injections). Doses may be given daily, unless untoward effects appear. If untoward effects appear, the drug should be given on alternate days, the dosage reduced, or administration stopped, as the circumstances indicate. The most frequent toxic effects are nausea and vomiting. In rare instances, increased fever, dizziness, urticaria, abdominal and muscular pain, renal irritation, and increased bleeding may appear. It is said that bronchitis and pneumonia may be made worse. A few cases of anaphylactic reaction have been reported.

c. Immediate results of treatment. The response to treatment may be dramatic, but it is usually slow. Reduction of the temperature to normal values may take a week or more, and reduction of the spleen is usually slower. When neostibosan is given in daily doses, the patient may show relatively little improvement until the course of treatment is nearly over. In the great majority of cases, however, improvement is then steady. The return of the white blood cell count to normal values is an important criterion of progress. Cures often result even though the response to treatment appears to be late.

d. Follow-up. The condition of the patient should be carefully appraised at the end of each week following treatment. As a rule, the minimum period of strict hospitalization should be 30 days from the end of treatment. A further convalescent period of at least 30 days is necessary in most cases. In the 4th week after completion of treatment, *Leishmania donovani* should be searched for again in suitable tissue. If parasites are found on this examination, or

symptoms and signs persist which are not otherwise explained, another course of treatment should be given. The length of a second course at this time should be decided by clinical judgment. When relapses occur, they usually appear within 6 months of treatment, but they may appear as much as a year later. The occurrence of a relapse should be established by parasitologic study. The development of cutaneous lesions containing Leishman-Donovan bodies should be considered as a relapse. Later courses are just as effective as first courses of chemotherapy, but in order to avoid failure a second time, consideration should be given to the need for larger doses and a longer course of neostibosan. At present, cure can be demonstrated only by follow-up. Individuals for whom a diagnosis of kala-azar has been established should be reexamined, if possible, every month for 6 months after disposition, and again at the end of a year.

8. PROGNOSIS. Death ensues in 75 percent or more of the untreated cases. When adequate treatment is instituted early in the course, and indicated repetitions of treatment are given, there should be practically no deaths from this disease. Most patients should be free of abnormal findings at the end of a month following treatment and in normal health at the end of another month. Relapses are estimated to occur in not over 5 percent of the cases in China and India; most of these cases are curable by further treatment.

9. PREVENTION. *a. General.* Although much remains to be learned about the transmission of kala-azar and the habits of species of *Phlebotomus* which may serve as vectors, certain effective measures based on present knowledge may be taken to prevent infection of troops with the disease. These include chiefly the segregation of troops at a safe distance from infected native populations, the control of sandfly vectors, and individual protection from the bites of sandflies. Many measures used in malaria control also afford protection against kala-azar.

b. Location of camps. Camp sites should be located on open, elevated, dry, sandy ground when feasible, and as far from native dwellings and domestic animals as possible. The more breeze in a given location, the better.

c. Protection of buildings. Ordinary screening does not exclude sandflies. Occupants of buildings may be effectively protected, however, by the application of DDT residual spray (QM Stock No. 51–I–305) to the entire inner walls, ceilings and fixtures, and to the inside and outside of screens and doors, including a foot or two of the outer wall around their casements. Sandflies entering buildings make frequent short flights along the walls and upon touching treated surfaces usually will be poisoned sufficiently to prevent their biting. Additional protection may be secured by spraying twice daily, at night and in early morning, with an aerosol dispenser or other available insecticide. These measures should be applied in sleeping quarters, shower rooms, latrines, mess halls, theaters, and other buildings where personnel congregate or work indoors at night. Buildings may be made less suitable as sandfly shelters by eliminating cracks and crevices in the walls, by reducing fixtures to a minimum, and by keeping clothing and duffle away from walls where sandflies may seek protection during the daytime.

d. Area control of sandflies. Whenever possible, the area within a radius of 50 to 100 yards of camp sites and quarters should be cleared of rubble, detritus, gardens, vegetation, and needless earthen walls or banks which may serve as breeding places or shelters for sandflies. When removal of vegetation is impractical, it may be sprayed with DDT solution from the ground at the rate of 2 to 4 pounds of DDT per acre, forming a barrier, as recommended against adult mosquitoes (see TB MED 110). To obtain area control, DDT residual spray should be applied to observed and potential *Phlebotomus* shelters and to resting sites on which sandflies alight when approaching a house, thus interposing a barrier between the breeding places of vectors and the dwellings to be protected. These include sites such as stone walls, masonry ruins, piles of stones, tree buttresses, caves, crevices, and animal burrows. When troop concentrations are necessarily in proximity to infected native populations, spraying of their dwellings with DDT residual spray is

advisable. DDT in oil, distributed by aircraft in amounts effective for mosquito control, also greatly reduces the sandfly population.

e. Sleeping nets. Standard mosquito netting does not keep out sandflies. Sleeping nets of mesh fine enough (more than 45 per inch) to keep out sandflies should be used in heavily infested areas, if other effective measures for protection are not feasible. When fine mesh nets are not available or are impracticable, treatment of nets of ordinary mesh with DDT or impregnation with insect repellent may be helpful in excluding sandflies.

f. Repellents. After sundown, quartermaster-issue insect repellent (QM stock No. 51–R–265) should be used on exposed parts of the body. Protection against bites of sandflies lasts for 4 to 6 hours. One application should be made at sundown and a second upon retiring. Regular use of repellent has proved an effective means of preventing sandfly bites.

g. Protective clothing. Long-sleeved shirts and full length trousers should be worn, especially after sundown.

h. Avoidance of exposure. Contact with native populations, which serve as the reservoir of infection, should be restricted to a minimum. Troops should be prohibited from visiting villages, particularly at night, when sandflies usually feed. Since dogs may serve as a source of infection, they should not be permitted around troop installations.

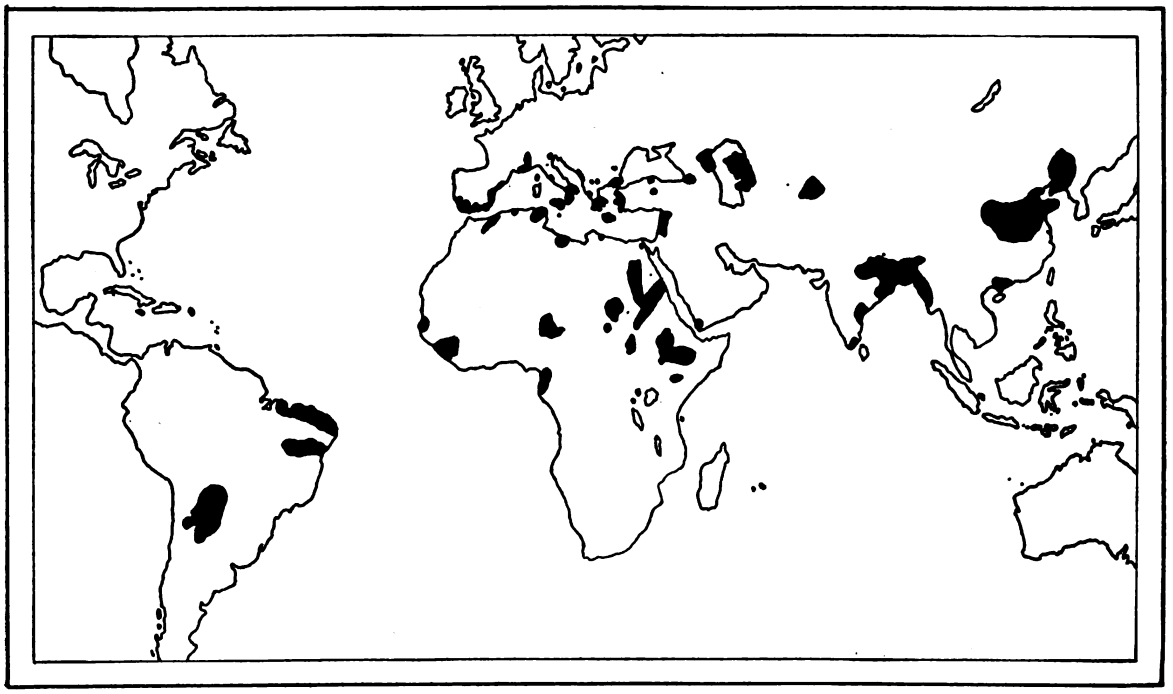

Figure 1. Distribution of visceral leishmaniasis.

Figure 2. Leishman-Donovan bodies of L. donovani *in stained smear from spleen puncture. (From Army Medical Museum collection.)*

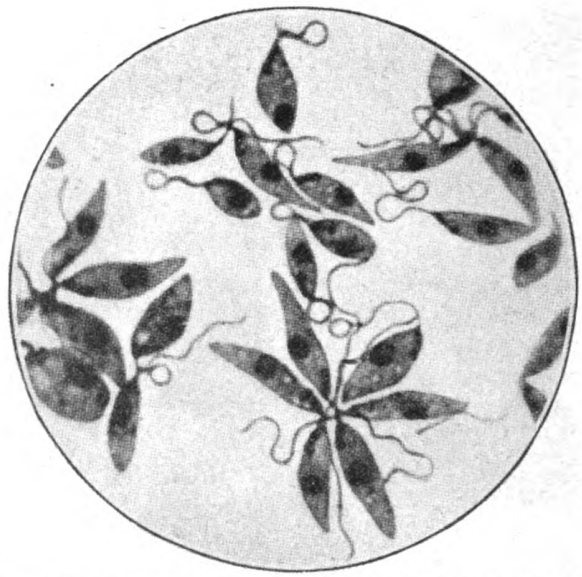

Figure 3.—Flagellate (leptomonad) forms of Leishmania *from culture. (From Army Medical Museum collection.)*

[AG 300.5 (14 Jul 45)]

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